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14. ABSTRACT

The purpose and scope of this proposal was to identify markers of postural instability associated with PD and to relate the objective measures of postural instability to clinical ratings of PD severity. Postural sway of PD patients was quantified using an array of linear and nonlinear measures. For H-Y Stage 2 patients postural sway variability and stationarity were able to differentiate PD patients from age-matched controls. For H-Y Stage 3, sway variability differentiated PD patients and controls. There was only one significant correlation, which was between the UPDRS posture score and the nonlinear measure of non-stationarity in the anterior-posterior direction. In spite of the limited sensitivity of the individual measures, stepwise regression revealed four postural sway measures that significantly predicted H-Y stage (anterior-posterior sway variability, sway path length, sway pattern complexity, and sway nonstationarity). Sway variability (AP) and sway nonstationarity significantly predicted the UPDRS posture scores. Those findings suggest PD severity may be objectively classified using multiple indices of postural sway activity.

15. SUBJECT TERMS
Parkinson's disease, movement disorders, postural control, balance, motor performance, posturography

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Introduction

Chronic postural instability is one of the primary symptoms of Parkinson's disease (PD). PD is a neurological movement disorder that affects an estimated 1.5 million Americans. VA Medical Centers treat over 40,000 patients with PD annually (Department of Veteran's Affairs, 2003). The identification of environmental factors as causes of PD and PD-like symptoms (Betarbet et al., 2000; Ghaemi et al., 2000; Rail et al., 1981) also has military significance. Warfighters who experience exposure to neurotoxins or infectious agents during a chemical or biological attack, or other personnel who are exposed to toxic agents as a consequence of military occupations, may be at risk for developing PD or similar neurological disorders. It is thus important to refine our understanding of the behavioral and neurological effects of PD and to develop objective diagnostic methods for the early detection of PD and related disorders (MOMRP Fact Sheet Number 7, 1999).

Balance problems related to PD typically present 5-6 years after initial symptom onset, and increase in severity as the disease progresses. Fall-related injuries and fear of falling are significant factors contributing to the reduced mobility that characterizes individuals with advanced PD. Despite the importance of balance problems associated with PD, current methods of clinically diagnosing postural instability associated with PD are somewhat crude and subjective, and little is known about factors that interact with PD-associated postural instability to further threaten balance. PD diagnosis and treatment would benefit from the ability to objectively detect postural instability at an earlier stage than is currently possible. The research reported herein has addressed that issue by employing *static posturography* (computerized measurement of *postural sway*—subtle, naturally occurring fluctuations of the body) to objectively quantify postural instability associated with different stages of PD severity.

The objective of this proposal was to identify markers of postural instability associated with PD and to relate the objective measures of postural instability to clinical ratings of PD severity, the Unified Parkinson's Disease Rating Scale (UPDRS; Fahn et al., 1987) and Hoehn-Yahr (H-Y; Hoehn & Yahr, 1967) mobility rating. We hypothesized that the postural sway of PD patients would be associated with increased variability and increased spatiotemporal regularity, relative to sway of healthy, age-matched controls, especially as clinically rated PD severity increased and under non-optimal conditions for maintaining posture (e.g., in the absence of visual information used to control stance or in conditions of reduced biomechanical stability). The specific aims of the proposal were to (1) Identify characteristics of postural sway associated with PD; and (2) Correlate clinical ratings of PD severity with objective posturographic measurements. We expected PD patients' sway to exhibit greater variability and greater

spatiotemporal regularity than that of age-matched controls, and that the difference will be greater for more advanced stages of PD, and that UPDRS scores would correlate positively with our innovative time-series measures of postural sway variability and spatiotemporal regularity.

Body

Research Protocol & Methods

All procedures were approved by U.S. Army and University of Cincinnati Institutional Review Boards, and all participants gave written informed consent and signed a HIPAA form before serving as research subjects. All research staff were trained and certified in HIPAA regulations. No adverse events involving human subjects occurred during the research project.

Participants. Postural stability was measured in 28 PD patients (mean age = 65.35 years, SD = 9.06 years, range = 48 – 80 years, 15 M, 13 F) who were recruited either from the Central Ohio Parkinson Society support group in Columbus, Ohio, or the Aring Neurology Clinic in the Department of Neurology at University Hospital in Cincinnati, Ohio. All PD patients who participated in this study were classified into one of four H-Y (Hoehn & Yahr, 1967) mobility classification stages: H-Y Stage 1: (n = 3 patients), H-Y Stage 2 (n = 17 patients), H-Y Stage 3 (n = 7 patients), and H-Y Stage 4 (n = 1 patient), as diagnosed by their treating neurologist. According to the H-Y classification system, Stage 1 represents early symptom appearance on one side of the body, Stage 2 represents bilateral symptoms but no postural instability, Stage 3 indicates the onset of physician-diagnosed postural instability (usually according to the retropulsion test—the patient is suddenly pulled backward and the physician determines the quality of the patients response, such as whether the patient began sustained backward stepping), Stage 4 indicates severe immobility, and Stage 5 indicates complete immobility (wheelchair bound). Our efforts to recruit approximately equal numbers of participants in H-Y Stages 1-4 were not successful, but the large sample of H-Y Stage 2 participants allowed for an interesting and important comparison of the objective, posturographic methods with the more subjective physician reports (H-Y stage and UPDRS scores), since H-Y Stage 2 patients are not supposed to exhibit marked postural instability.

The PD patients reported their medication regime and were asked to participate in the study during an "on" phase of the medication cycle (the time after dosage at which symptoms are most well controlled by the medication). Additional patient information collected from physicians during participant recruitment included disease duration (mean = 7.6 years), symptoms of bradykinesia and dyskinesia, rigidity and rest tremor during examination, patient reports of on-off fluctuations in medication cycles, the UPDRS score (mean = 29.5, 21.80, and 0.82 for the motor subscale, and posture scores, respectively), and observations of freezing gait (see Appendix 1 for a blank physician information form collected

for participants). Physician-observed postural instability (i.e., results of the retropulsion test) was also obtained for each PD participant.

Postural stability measures obtained from PD patients were compared to stability measures taken from 17 elderly, healthy controls (5 M, 12 F; mean age = 66.0 years, SD = 9.59 years, range = 48-80 years). Participants with a history of diabetes, arthritis or other illnesses affecting balance, a recent injury, vestibular disorder, dizziness, a history of falls, heavy use of alcohol or other drugs, or chronic back pain were excluded from the study.

Apparatus. Postural stability data were obtained in this study using an AccuSway Plus portable force platform with *Balance Clinic* software (Advanced Medical Technologies, Inc., Waterton, MA) running on a laptop PC. Data were sampled at 100 Hz. *Balance Clinic* was used to compute anterior-posterior (AP) and medio-lateral (ML) center-of-pressure (COP) time series from the force platform recordings.

Procedure. Within-subjects manipulations of vision (eyes open vs. eyes closed) and stance (feet apart vs. feet together) were factorially combined, yielding four experimental conditions (eyes open/feet apart; eyes open/feet together; eyes closed/feet apart; eyes closed/feet together). Those manipulations were intended to result in balance conditions that varied in difficulty, with eyes open/feet apart representing the easiest and eyes closed/feet together representing the hardest condition. Each condition was repeated two times, resulting in eight trials per participant. Conditions were presented in completely randomized order. Testing sessions lasted approximately 15 minutes.

After removing their shoes, participants were instructed to stand on the force platform in a relaxed stance, with their arms suspended naturally and comfortably at their sides. They were further instructed not to speak, gesture, or make any large-scale voluntary movements (e.g., of the arms) during the postural stability measurement period. At the beginning of each trial, participants assumed the appropriate stance and vision condition according to instructions, and data collection began once the participant indicated he or she felt stable and ready to begin. Two experimenters were present on either side of the participant for safety purposes. Each trial lasted 30 seconds. Participants stepped off of the force platform for a brief period between each trial. Participants were allowed to sit for rest breaks as needed.

Data Reduction and Analysis

AP and ML COP time series were reduced to yield the following summary statistics to characterize postural sway:

- SD (standard deviation of the COP): a measure of postural variability

- LSD (local standard deviation; McNevin & Wulf, 2002; Mitra, 2004; Riley, Stoffregen, Grocki, & Turvey, 1999): a fine-grained variability measure obtained by computing the SD over non-overlapping 1 second data windows, and then averaging the SD values across windows

- PL (path length): the total distance covered by the COP over the 30 second trial

The AP and ML COP time series were also submitted to a nonlinear time series analysis termed recurrence quantification analysis (RQA; Pellecchia & Shockley, 2005; Webber & Zbilut, 1994, 1996, 2005; Riley, Balasubramaniam, & Turvey, 1999; Schmit et al., in press). RQA detects subtle, time-correlated (i.e., recurrent or repeating) patterns in the data and yields the following quantitative indices of the time evolution of the COP:

- %Recurrence: a measure of the extent to which values in the time series repeat themselves at different times

- %Determinism: a measure of the extent to which the repeating values tend to repeat as strings of data, indicating the presence of deterministic (predictable, non-random) rules that govern the temporal evolution of the data

- Entropy: a measure of the complexity of the deterministic structure of the time series. Greater entropy reflects greater variety in the distribution of repeated strings of data.

- Trend: a measure of the extent to which the time series is nonstationary

RQA involves embedding the time series in spaces of multiple dimensions. Dimensions were constructed using the method of delays (Abarbanel, 1996) in which time-delayed copies of the original time series serve as surrogate dimensions. In the present study, eight embedding dimensions were used, constructed with a time-delay factor of 8 data points. The inclusion radius used for determination of whether points in embedded space were recurrent was 20% of the mean Euclidean distance separating all points in the space (see Riley et al., 1999, and Pellecchia & Shockley, 2005).

Pearson correlations between the postural sway measures and the patients' UPDRS motor-subscale and postural stability item scores were computed to determine the degree of association between the clinical and posturographic measures. It is not customary for physicians to complete all UPDRS items for PD evaluation so total UPDRS scores were not provided to us. Correlations between the continuous postural sway measures and the categorical H-Y stage values for each participant were also computed. Finally, we performed stepwise

multiple-regression analyses to determine which posturographic measures predicted clinical ratings of PD severity.

Results

Comparison of Participant Groups and Effects of Experimental Factors. Due to the small sample sizes in H-Y stages 1 (n = 3) and 4 (n = 1), we were unable to use H-Y stage as a factor in an omnibus analysis of variance (ANOVA) to compare all stages of PD severity represented in our sample. Instead we submitted the data from H-Y stages 2 (n = 17) and 3 (n = 7) and corresponding age-matched controls to separate three-factor (*Group* × *Stance* × *Vision*) mixed-design ANOVAs. For H-Y stage 2, there were only two significant effects involving *Group* (Stage 2 PD vs. controls). The first significant effect was an interaction between the influences of *Group* and *Stance* on *SD-ML* (see Figure 1A), $F(1, 32) = 6.92$, $p < .05$. Simple-effects ANOVA revealed that with feet-apart, *SD-ML* was greater for PD than control participants, $F(1, 32) = 8.88$, $p < .01$, but there was no difference between PD and controls with feet-together ($F < 1$). The other significant effect involving *Group* was an interaction between *Group* and *Vision* on *Trend-AP* (see Figure 1B), $F(1, 32) = 5.78$, $p < .05$. Simple-effects ANOVA revealed that with eyes-open, *Trend-AP* was greater in magnitude for PD than for controls, $F(1,32) = 5.24$, $p < .05$ (controls exhibited greater non-stationarity than PD). For eyes-closed, there was no difference between groups ($F < 1$).

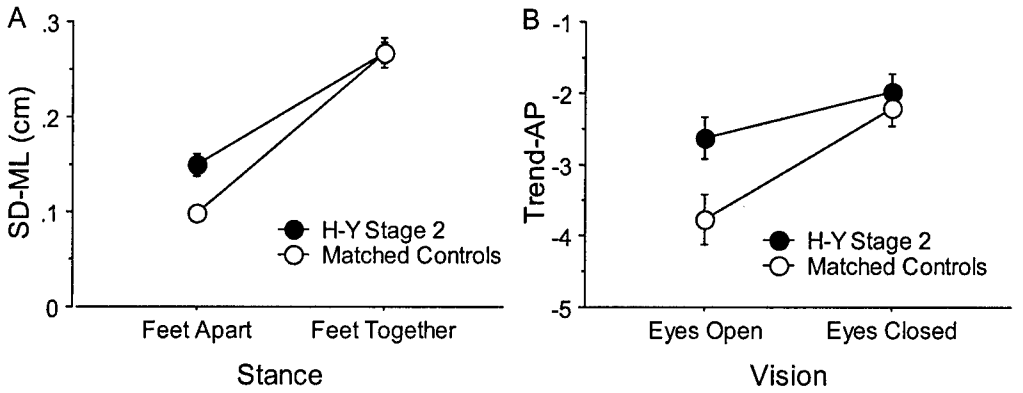

Figure 1. A) Standard deviation of center of pressure in the mediolateral direction as a function of stance. B) Trend (non-stationarity) in center of pressure as a function of vision

For the comparison of H-Y stage 3 PD patients to controls, the only significant effect was a main effect of *Group* on *SD-AP*, $F(1,12) = 6.98$, $p < .05$. *SD-AP* was greater for PD than age-matched controls (see Figure 2).

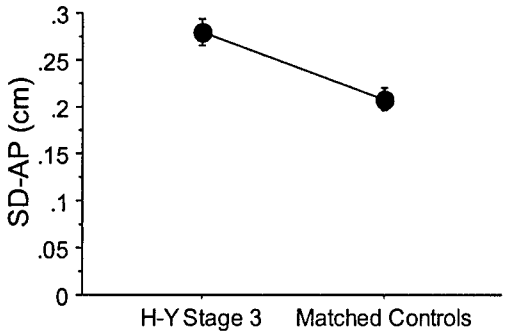

Figure 2. Standard deviation of center of pressure in the anterior-posterior direction as a function of participant type.

Correlations Between Postural Sway Measures and Clinical Ratings. Correlations between H-Y Stage (Coded 0 = Matched Controls, 1-4 for H-Y Stages 1-4, respectively), UPDRS Posture and Motor sub-scales may be found in Table 1. We found only one significant correlation, which was between *Trend-AP* and the UPDRS posture subscale. This correlation indicates that as posture becomes more compromised (indicated by a higher UPDRS posture score) the postural activity becomes more stationary. This finding is consistent with our hypothesis that increasing postural instability due to PD simultaneously yields more regular (i.e., stationary) postural sway patterns.

Predictive Usefulness of Postural Sway Measures. The data were submitted to stepwise multiple-regression analyses to identify which of the 13 measures of postural sway measures are predictive of H-Y Stage, UPDRS-Posture item, and UPDRS-Motor subscale. For prediction of H-Y Stage, SD-AP was the first significant factor and accounted for 9.3% of the variance in H-Y stage. Entropy-AP was the next significant factor, and accounted for an additional 4.9% of the variance in H-Y stage. The third significant factor in the model was PL, which accounted for 3.2% more variance. The final significant factor in the model was Trend-AP, which accounted for 3.3% more variance in HY stage. The model H-Y Stage = 10.541(SD-AP) – 0.043(PL) – 0.707(Entropy-AP) + 0.157 (Trend-AP) + 4.379 accounted for a total of 21.7% of the variance in H-Y Stage and was statistically significant ($p < .01$). The results indicated that SD-AP is positively related to H-Y stage. This finding is consistent with prior studies indicating that progression of PD results in increased postural instability (Contin et al., 1996; Diener et al., 1984; Rocchi et al., 2002; Schieppati et al., 1994; Schmit et al., in press;). The fact that PL and Entropy-AP were negatively related to H-Y stage is consistent with the results of Schmit et al. (in press), who found that Stage 3 PD patients exhibited a more regular (i.e., less complex) pattern to their postural sway trajectories. Non-zero values of Trend indicate

Table 1. Correlations between clinical ratings of PD severity (H-Y stage and the UPDRS posture and motor sub-scales) and the 13 posturographic measures.

Dependent Measure	H-Y Stage	UPDRS-Posture	UPDRS-Motor
SD-ML	.193	.214	.053
SD-AP†	.084	.202	-.003
Path Length†	.136	.192	.114
Local SD-ML	.119	.167	.007
Local SD-AP	.124	.273	.158
%REC-ML	-.027	-.072	.096
%REC-AP	-.173	-.262	-.151
%DET-ML	-.026	.021	-.020
%DET-AP	.007	.044	.064
Entropy-ML	-.023	-.015	-.012
Entropy-AP†	.171	-.153	-.069
Trend-ML	-.062	.076	-.038
Trend-AP†	.181	.308*	.158

* = significant correlations at the $p < .05$ level.
† = significant factor in stepwise multiple regression.

non-stationarity (drift in the mean state of the postural trajectory). The fact that *Trend-AP* is positively related to H-Y Stage is suggestive that the postural sway patterns of PD patients show less drift (greater stationarity) than non-PD individuals. The findings of Schmit et al. (in press) and our hypothesis that PD patients' postural sway pattern become more regular (i.e., more deterministic or predictable) is also consistent with this finding.

For prediction of UPDRS-Posture, Trend-AP was the first significant factor, accounting for 7.9 % of the variance in UPDRS-Posture scores. The other significant factor was SD-AP, which accounted for an additional 5.4% of the variance in UPDRS-Posture scores. The model UPDRS-Posture = 2.77(SD-AP) + 0.172(Trend-AP) + 0.514 accounted for a total of 13.3% of the variance in UPDRS-Posture scores and was significant ($p < .01$). Once again, the positive relationship between UPDRS-Posture scores and SD-AP is consistent with

previous and current findings that progression of PD results in progressively more postural instability.

There were no significant factors for the prediction of UPDRS-Motor scores.

Key Research Accomplishments

We achieved the specific aims of the proposal. The key accomplishments of this research were:

- We identified features that distinguished PD patients from healthy, age-matched control participants.
    - ANOVAs revealed that H-Y Stage 2 PD patients exhibited greater mediolateral sway variability than controls when participants stood in the more stable feet-apart condition, but the groups did not differ in the less stable feet-together condition. The H-Y Stage 2 PD patients also produced more stationary postural sway time series than controls when standing with the eyes open, but the groups did not differ when standing with the eyes closed. These are important results, because according to the H-Y mobility classification scheme postural instability is not supposed to be present at Stage 2. These results suggest that the objective, quantitative posturographic measures may be more sensitive to subtle disturbances of postural sway than the clinical ratings.
    - ANOVA s revealed that H-Y Stage 3 PD patients exhibited more anterior-posterior postural sway variability than controls, consistent with our previous results (Schmit et al., in press).
    - Stepwise multiple regressions identified patterns of postural sway descriptors that predicted clinical ratings of disease severity. The significant model *H-Y Stage = 10.541(SD-AP) – 0.043(PL) – 0.707(Entropy-AP) + 0.157 (Trend-AP) + 4.379* accounted for a total of 21.7% of the variance in H-Y Stage, and the significant model *UPDRS-Posture = 2.77(SD-AP) + 0.172(Trend-AP) + 0.514* accounted for a total of 13.3% of the variance in UPDRS-Posture scores.
- We computed simple correlations between individual posturographic measures and clinical ratings of PD severity. Of the 13 measures, the only significant correlation was between Trend-AP the UPDRS-Posture score. Increasing postural sway nonstationarity in the anterior-posterior sway axis is related to clinical ratings of the severity of postural instability associated with PD.

- Preparation of a manuscript reporting the results of the funded research over the past year has just begun after the close of the data collection period (Riley, Shockley, & Baker, in preparation).

Reportable Outcomes

- The grant support facilitated the revision of a manuscript (Schmit et al., in press, *Experimental Brain Research*) reporting the preliminary data on balance control and PD that was described in the original proposal.

- We formed a partnership with the Central Ohio Parkinson's Society to facilitate recruitment of research participants and to disseminate research results and information about postural instability in PD directly to PD patients and caregivers.

- Aimee Baker (graduate research assistant) was selected to attend the Motor Control Summer School at Penn State University in June 2005. Course modules on Parkinson's disease and on new data analysis techniques and theories and concepts from the wide range of multi-disciplinary approaches to studying human movement (neurophysiological, mathematical, psychological, biomechanical) were taught. This experience contributed to the depth of knowledge and skill set of our PD research team.

- Training of an undergraduate research assistant (Christi Brandenburg) was supported

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Schmit, J. M., Riley, M. A., Dalvi, A., Sahay, A., Shear, P. K., Shockley, K. D., & Pun, R. Y. K. (in press). Deterministic patterns of postural sway in Parkinson's disease. *Experimental Brain Research*.

List of Personnel Receiving Pay

Michael A. Riley, Ph.D. (PI)
Kevin Shockley, Ph.D. (Co-PI)
Jennifer Schmit, M.A. (GA)
Aimee Baker, B.A. (GA)

Conclusions

Our overarching goal of the proposal *Objective Markers of Postural Instability in Parkinson's Disease*—to identify objective indicators of postural instability in Parkinson's Disease—was accomplished by identifying four dependent measures that, in combination, were predictive of clinical ratings of PD severity. It is important to note that only one of these measures (nonstationarity in postural sway) was alone significantly correlated with PD severity and only with the UPDRS posture score. This suggests that PD severity (and, possibly, disposition toward PD) is most readily characterized by an array or profile of measures rather than by any single measure. Furthermore, our findings are indicative that conventional and nonlinear measures of postural sway activity complement one another with respect to characterizing the nature of postural sway changes resulting from PD. Future longitudinal research is indicated to determine the extent to which the present objective parkers of postural instability in PD are useful in predicting risk of PD.

The identification of differences between H-Y Stage 2 PD patients and healthy control participants is important. As noted, the H-Y mobility classification scheme postural instability is not supposed to be present at Stage 2. These results suggest that the objective, quantitative posturographic measures may be more sensitive to subtle disturbances of postural sway than the clinical ratings. This suggests that the measures may have some value in predicting postural instability and in serving as early screening tools. Those possibilities remain to be evaluated in future research.

Our results are also consistent with the findings of Schmit, et al. (in press), who found that variability in postural sway was greater for PD than controls, but that the postural sway was more regularly (deterministically) patterned than the postural sway of age-matched controls. This finding may reflect a more general pattern that has recently gained notice in the literature (e.g., Goldberger, 1996, 1997; Goldberger, Peng, & Lipsitz, 2002; Goldberger, Rigney, & West, 1990; West & Goldberger, 1987), namely that high regularity in physiological and behavioral patterns is indicative of pathology. For example, cardiac rhythms associated with a healthy state exhibit complex patterns of variability, whereas cardiac rhythms associated with pathology exhibit a tendency for simple, regular, deterministic patterns. Irregular patterning in biological activity may characterize states of relative health and reflect flexibility in the system and exploration of functional dynamical space. When biological systems are compromised by pathologies this healthy, variable dynamical regime is highly restricted and rendered rigidly ordered. Such a restriction may be an adaptive response to pathology, though it is not yet clear in what way this functional change might be adaptive.

The continued development of sensitive, objective techniques of diagnosing postural instability, coupled with an understanding of the factors that modulate

postural instability, will reduce the incidence of falls and loss of mobility associated with PD. Such research will also contribute to establishing posturography as a method of evaluating PD treatments and, importantly, contribute to the development of data-driven techniques (e.g., artificial neural network models) that allow for the early diagnosis of PD and related pathologies.

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Appendices

Appendix 1: Physician Information Form
Appendix 2: Schmit et al. (in press) pre-print

APPENDIX 1

PLEASE RETRIEVE INFORMATION FROM PATIENT VISIT ON OR BEFORE (CLOSEST TO): _____

PARTICIPANT ID: _____

DOB: _____

DURATION OF DISEASE (YRS): _____

DOES PATIENT EXHIBIT:		
Bradykinesia	YES	NO
Dyskinesia	YES	NO
On-Off fluctuations	YES	NO
Freezing	YES	NO
Rest Tremor	YES	NO
Postural Instability	YES	NO

HOEHN AND YAHR STAGE SCORE: (circle one)	
I	Unilateral disease
II	Bilateral disease without postural instability
III	Postural instability
IV	Severe disability; able to walk/stand unassisted
V	Wheelchair bound or walking only with assistance.

MEDICATION	DOSE

TOTAL UPDRS SCORE:
_____ / _____

MOTOR SUBSCALE:
_____ / _____

UPDRS

Postural Stability Item – Retropulsion Test (circle one)	
0	Normal
1	Recovers unaided
2	Would fall if not caught
3	Falls spontaneously
4	Unable to stand

Please return via fax (513.556.1904) or mail (Michael A. Riley, Ph.D., Department of Psychology, ML 0376, 429 Dyer Hall, University of Cincinnati, Cincinnati, OH, 45221-0376).

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APPENDIX 2

RESEARCH ARTICLE

~~COP dynamics in Parkinson's disease~~~~Deterministic~~Deterministic center of pressure patterns characterize postural instability in Parkinson's disease

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Abstract Static posturographic recordings were obtained from six Parkinson's patients and six age-matched, healthy control participants. The availability of vision and visuo-spatial cognitive load were manipulated. Postural sway patterns were analyzed using recurrence quantification analysis (RQA), which revealed differences in center of pressure (COP) dynamics between Parkinson's and control participants. AP COP trajectories for the Parkinson's group were not only significantly more variable than for the control group, but also exhibited distinct patterns of temporal dynamics. The visual manipulation did not differentially affect the two groups. No cognitive load effects were found. The results are generally consistent with the hypothesis that pathological physiological systems exhibit a tendency for less flexible, more deterministic dynamic patterns.

Keywords Parkinson's disease · Postural control · Balance · Posturography · Recurrence quantification analysis

Introduction

Postural instability is a primary symptom of Parkinson's disease (PD) and often leads to falls or a fear of falling, both of which limit mobility and reduce the quality of life for patients (Adkin et al. 2003; Koller et al. 1989; Stolze et al. 2004). Despite the prevalence and importance of postural instability in PD, knowledge of the nature and source of postural instability remains limited. One reason is that empirical findings regarding postural instability in PD have been contradictory. Some studies found a decrease in postural sway variability for PD patients relative to controls (Horak et al. 1992; Schieppati and Nardone 1991), but other studies found an increase (Contin et al. 1996; Mitchell et al. 1995; Rocchi et al. 2002; van Wegen et al. 2002; Viitasalo et al. 2002). A second reason is that very little is

known about dynamic, temporal patterns of postural sway in PD (Maurer et al. 2004; Mitchell et al. 1995). Knowledge of postural sway dynamics in PD can provide new insights into the nature of the disease process that may be unattainable using measures that ignore or average over the time-evolving properties of sway (Milton and Black 1995; Vaillancourt and Newell 2002; van Emmerik and van Wegen 2000). Measures of the latter type include standard measures of postural sway variability, such as the standard deviation or root mean square sway variability of the center-of-pressure (COP). The primary goal of the present study was to characterize dynamic COP patterns in PD.

Postural sway dynamics in PD

Mitchell et al. (1995) employed stabilogram-diffusion analysis (SDA; Collins and De Luca 1993, 1995; Riley et al. 1998) to characterize dynamic patterns of COP time series in PD. SDA quantifies the amount of stochastic activity (the diffusion coefficient, D) and the strength and direction (positive or negative) of temporal correlations (the Hurst exponent, H) over short ($< \sim 1$ s) and long ($> \sim 1$ s) time-scales. According to Collins and De Luca's original model those two correlation regimes map to a two-part control system, with an open-loop controller operating over the short time-scale and a closed-loop controller operating over the longer time-scale (the interpretation of SDA results as reflecting open-loop and closed-loop control regimes is no longer widely accepted, however; see Dijkstra 2000; Newell et al. 1997; Peterka 2000; Riley et al. 1998). Mitchell et al. found that D over the short time-scale was higher, and that the transition point between the two regimes was greater, for PD patients relative to control participants. They found no differences in H across groups. Similar results were obtained by Rocchi et al. (2004) using a variant of SDA. Mitchell et al. interpreted their results as consistent with a proposed compensation for postural inflexibility (Horak et al. 1992; Melnick et al. 1999; Schieppati et al. 1994). They also interpreted their results in terms of the Collins and De Luca model as indicating that PD is associated with a higher threshold for the amount of short time-scale, open-loop sway that is tolerated before the closed-loop control system initiates corrective responses. Maurer et al. (2004) replicated the finding of a higher transition threshold, and also observed that the COP of PD patients exhibited an abnormal oscillation at ~ 1 Hz. Based on their time-delay sensory feedback model, they concluded that postural sway in PD could reflect higher levels of neuromotor noise and variations in the motor gain of a feedback loop.

Time series of a variety of physiological variables associated with different pathological states have been shown to exhibit a loss of complexity (Goldberger 1997; Goldberger et al. 2002). The complexity loss may be expressed in two ways: (1) as increasingly regular or deterministic (often periodic) temporal dynamics, or (2) as increasing randomness or a loss of long-range correlations. The presence of postural inflexibility and a 1 Hz sway oscillation in PD suggests that postural sway in PD will exhibit a loss of complexity consistent with the first of those forms—postural sway dynamics will exhibit a tendency for increased regularity or determinism. One of the aims of this study was to investigate whether greater determinism in the temporal structure of COP time series would be found for PD participants.

We used recurrence quantification analysis (RQA; Webber and Zbilut 1994, 1996) to evaluate the hypothesis of increased COP determinism associated with PD. RQA has exhibited sensitivity to changes in postural sway dynamics in response to variations in the availability of sensory information used to control balance (Riley et al. 1999; Riley and Clark 2003), to supra-postural behavioral (Balasubramaniam et al. 2000), and cognitive constraints (Riley et al. in press), and to balance expertise (Schmit et al. in press). We chose to use RQA rather than SDA to characterize COP dynamics because SDA has not exhibited sensitivity to changes in the complexity of COP time series in PD patients (H has not been found to differ for PD patients and controls). Moreover, the numerical methods and postural control models associated with SDA have received criticism (Chiari et al. 2000; Delignieres et al. 2003; Dijkstra 2000; Newell et al. 1997; Peterka 2000; Rougier 1999), and related analyses (Blaszczyk and Klonowski 2001; Duarte and Zatsiorsky

2000, 2001) seem to tell a different story than the original Collins and De Luca (1993) method with regard to the presence of two distinct scaling regions.

Specific predictions about COP dynamics in PD were derived from joint consideration of the loss-of-complexity hypothesis (Goldberger 1997; Goldberger et al. 2002; Vaillancourt and Newell 2002) and the well-known inflexibility, stereotypy, and rigidity of action that characterizes PD (van Emmerik and van Wegen 2000). Among the characteristics of a time series that RQA quantifies is the amount of deterministic structure (the inverse of the amount of randomness), which is measured by *\% determinism* (the extent to which series of data points repeat themselves along the time series). The primary hypothesis was that PD participants would exhibit higher % determinism than controls. We also expected PD patients to exhibit greater nonlinear auto-correlation of the COP (measured by *\% recurrence*, the extent to which the data series repeats itself over time, whether as series of data points or as individual data points), greater mathematical stability of the COP (measured by *maxline*; systems with greater mathematical stability—which is not equivalent to postural stability, but refers to the response of a trajectory to a slight change in initial conditions—exhibit less behavioral flexibility than systems with less mathematical stability; see Kelso 1995; van Emmerik and van Wegen 2000), and greater COP stationarity (lower magnitude of *trend*). That pattern of results would indicate that postural control in PD is characterized by rigid, inflexible, and less complex modes of behavior. We made no predictions regarding *entropy*, which is reported to be a measure of the complexity of the deterministic dynamics of a time series (Webber and Zbilut 1994). COP entropy might be expected to decrease in PD given the loss-of-complexity hypothesis, but the RQA variable entropy is essentially a measure of the regularity of deterministic strings of data in a time series. Goldberger et al. (2002) cautioned against the use of regularity measures for evaluating the loss-of-complexity hypothesis, since regularity and complexity are not equivalent concepts.

Postural control and cognitive activity

The relation between cognition and postural control has received considerable attention recently (Woollacott and Shumway-Cook 2002). Cognitive load during standing may be especially relevant for people with PD, since they seem less able to adaptively prioritize the execution of concurrent behaviors in a way that preserves postural stability (Bloem et al. 2000) and since they may use explicit, compensatory, cognitive strategies to maintain balance (Morris et al. 2000). Morris et al. found, using a variety of clinical assessments, a decline in balance performance during cognitive activity for people with PD. However, they did not quantify postural performance objectively using a device such as a force platform. Marchese et al. (2003) used a force platform to quantify postural activity during concurrent cognitive activity and found an increase in COP area and path length for PD participants during dual-task conditions. However, their cognitive task condition was confounded by the fact that participants counted aloud to perform the cognitive task condition but did not vocalize during the no-task control condition. Vocalization introduces biomechanical and respiratory artifacts in postural measurements (Dault et al. 2003). We used a cognitive task that did not require vocalization. We selected a visuo-spatial task because PD participants may exhibit increased reliance on vision for postural control (Bronstein et al. 1990). A visuo-spatial cognitive task might therefore be expected to have a greater effect for PD participants than would a non-visual task, and have a greater effect on PD than control participants. We also expected that any differences between PD and control participants would be exaggerated for the cognitive-task trials. To further explore the interplay between visuo-spatial cognitive demand and visual control of posture we also manipulated the availability of vision—participants stood with the eyes either open or closed.

Methods

Participants

Six PD patients (mean age = 70.83 years, SD = 15.89 years, range = 40–83 years; two males, four females) who were receiving treatment at University Hospital (Cincinnati, OH, USA) participated. Patients were staged by their neurologists (the third and fourth authors) according to the H-Y (Hoehn and Yahr 1967) mobility classification at Stage 3. H-Y stage 3 is defined by the presence of postural instability, determined typically using the retropulsion or "pull" test. PD patients participated in the study during the self-determined peak on-phase of the medication cycle. Six elderly, healthy controls (mean age = 70.17 years, SD = 4.71 years, range = 64–77 years; two males, four females) also participated. Participants were screened to exclude individuals with a history of diabetes, arthritis, a recent injury, vestibular disorder, dizziness, a history of falls, closed head injuries with prolonged loss of consciousness, heavy use of alcohol or other drugs, chronic back pain, or other conditions affecting balance.

Additional patient details are presented in Table 1. The clinical features noted in Table 1 were observed during patients' visits to their neurologist in the on-medication state. The symptoms were not necessarily observed during their most recent examination or during postural testing, but were observed at some point in the course of the patient's PD history. Postural testing generally occurred within 1–2 weeks of the most recent clinical examination. The first author was present during both the clinical evaluations and postural testing sessions and determined that none of the patients exhibited tremor or dyskinesia during testing.

All PD patients were prescribed dopaminergic therapies, including variations of Sinemet, Comtan, and Amantadine, and were on stable doses of medication for 3 months prior to the study. Because Levodopa sometimes induces confusion (Foltynie et al. 2002), and since we were interested in the effects of cognitive demand, we established a criterion level of cognitive functioning using the Folstein Mini-Mental State Examination (MMSE; Folstein et al. 1975). The MMSE was administered to all participants prior to postural stability testing. All participants met the criterion of MMSE $\geq$ 25/30.

Apparatus

Postural data were obtained using a Bertec 4060-NC force platform and Bertec AM-6701 amplifier (Bertec Corporation, Columbus, OH). The force platform system implemented a low-pass, anti-aliasing hardware filter with a cut-off frequency of 500 Hz. No other filtering or signal conditioning algorithms were applied to the raw data. Data

Table 1 Patient summary "×" indicates presence of symptom during clinical examinations by the patient's neurologist (but not necessarily during postural testing)

Characteristic	S1	S2	S3	S4	S5	S6
Duration of disease (years)	8	5	6	6	5	7
Age (years)	77	83	78	79	68	40
Rigidity	×	×	×	×	×	×
Bradykinesia	×	×	×	×	×	×
Dyskinesia	×			×		×
Tremor	×	×	×	×	×	×
On-off fluctuations	×			×		×
Freezing	×			×	×	
Postural instability	×	×	×	×	×	×
Medications	SIN-CR, SIN, COMT, SYMM	SIN, REQ	SIN-CR, SIN	SIN-CR, SIN, REQ	SIN, REQ	SIN, REQ, COMT

SIN, SINEMET (Carbidopa/Levodopa); SIN-CR, SINEMET CR (Controlled Release Carbidopa/Levodopa); REQ, REQUIP (Ropinirole); SYMM, SYMMETREL (Amantadine); COMT, catechol- *O*-methyl transferase inhibitor

were sampled at 100 Hz. A PC and *Datapac 2000* software (Run Technologies, Inc., Mission Viejo, CA, USA) were used for data acquisition and COP calculations.

For protection in the event of a fall participants wore a vest-style, full-body safety harness that was anchored to the ceiling (no participants fell or lost balance during testing). Participants stood 1.23 m from a 36.8 × 25.4 cm^2 flat-panel monitor mounted on an adjustable stand at each participant's eye height, which was used to display cognitive task stimuli generated by a Silicon Graphics workstation. Cognitive stimuli (described below) were, on average, 11.38 × 10.03 cm^2 and subtended 5.29° of vertical and 4.67° of horizontal visual angle.

Procedure

Within-subjects manipulations of vision (eyes open, eyes closed) and cognitive demand (no-task, visuo-spatial cognitive task) were factorially combined, yielding four conditions. Each condition was repeated four times, resulting in 16 randomly ordered trials per participant. Testing sessions lasted approximately 1 h. Participants were allowed to rest as needed. All participants signed a written informed consent document. The study protocol was approved by the University of Cincinnati Institutional Review Board.

At the beginning of each trial, participants stood on the force platform in a natural stance, with the feet positioned shoulder-width apart. They were directed to relax and allow the arms to suspend naturally and comfortably at their sides. Participants were instructed not to speak, gesture, or make any large-scale voluntary movements during trials. A given trial began following notification from the participant of readiness to begin the trial.

On half the trials (randomly ordered), no cognitive task was performed. On remaining trials, a visuo-spatial cognitive task was performed. Participants were encouraged to perform the cognitive task as accurately as possible. Participants viewed a depiction of a 3-D object ("mental rotation" figures introduced by Shepard and Metzler 1971) on the monitor for 10 s prior to postural sway measurement. Novel figures were used on each cognitive task trial for a given participant. Each participant was presented the same set of figures, in a different random order. After 10 s, the figure disappeared. Depending on the randomly ordered vision condition, which was announced by the experimenter prior to the beginning of the trial, participants then either closed their eyes or kept them open. Acquisition of 30 s of postural data then commenced. Participants were instructed to stand comfortably during data acquisition while visually "rehearsing" or visualizing the shape. During eyes-open trials participants were not instructed to fixate any particular object or location in the room, but just to look ahead. After the 30 s data collection period ended, participants were instructed to again look at the monitor, where a second figure appeared, and to determine if the second figure was the same as the first figure by giving a "same" or "different" verbal response. On half of the cognitive task trials (randomly ordered) the second figure was the same as the first. In order to increase the demand of the task and to encourage participants to continuously and deeply concentrate on the object's shape during the posture data collection period, the second figure was visually identical to the first on half of the "same" trials, but rotated about all three spatial axes for the remaining "same" trials. If the second figure was identical to the first but rotated, a correct response was "same." Participants were not provided information about the proportion of trials on which the second figure was the same, nor were they explicitly instructed to perform mental rotations during the 30 s data collection period, but they were informed that the second figure could be a rotated version of the first figure. On trials when no cognitive task was performed, no stimuli were displayed on the monitor and participants were instructed to stand comfortably with their eyes open or closed while postural data were collected. Figure 1 depicts the experimental procedure.

Data analysis and reduction

There were two primary sets of dependent measures. The first set consisted of the within-trial SD of the anterior-posterior (AP) and medio-lateral (ML) COP time series (measures of postural sway variability) and COP path length (a measure of the amount of postural sway). Those measures were computed by *Datapac 2000*. The second set consisted of the multiple indices of the temporal dynamics of sway provided by RQA, including measures of the degree of nonlinear auto-correlation (% recurrence), randomness (% determinism), complexity/regularity (entropy), mathematical stability (maxline), and nonstationarity (trend). RQA requires the specification of input parameters related to an intermediate analysis stage (phase space reconstruction) and related to determining thresholds for identifying recurrent (repeating) data (for detailed descriptions of those parameters and for suggested methods to choose them see Pellechia and Shockley 2005; Riley et al. 1999; Webber and Zbilut 1994, 1996, 2005). We performed extensive preliminary data analyses using a wide range of parameter settings in order to identify a suitable set of input parameters. The final parameter settings we chose for both AP and ML time series were: embedding dimension = 8, time-delay = 9 samples, radius = 32% of the mean Euclidean distance separating points in the reconstructed phase space, and number of successive points defining a line segment = 2. These parameters yielded recurrence plots that were sparse (not saturated with recurrent points) but that contained enough recurrent points to reliably compute the RQA dependent variables. It should be noted that the selection of proper input parameters for RQA can be challenging, and there is no simple method that always allows determining the "correct" value of a given input parameter (nor are there universal criteria for establishing what makes one parameter setting correct and other settings incorrect; see Iwanski and Bradley 1998). The pattern of results we obtained was consistent across a range of parameter settings.

To rule out the possibility that the postural sway data appeared to contain deterministic dynamic patterns by chance, we compared our RQA results to results obtained from analyzing randomly shuffled COP data. COP time series were randomly re-ordered to create new time series with the same mean, variance, etc.—the temporal order of the data was destroyed but other statistical properties were preserved (see Theiler et al. 1992). Data shuffling resulted in substantial drops in the RQA measures (e.g., determinism for all shuffled trials was less than 1%), and recurrence plots of the shuffled data exhibited homogenous typologies and did not resemble plots for intact data. The outcome of this procedure indicated that our results reflected genuine properties of the temporal evolution of the COP, rather than spurious artifacts. This technique does not, however, guarantee optimality of the selected input parameters.

Dependent measures were averaged over repeated trials in the same condition to yield for each participant one average value of each of the eight dependent measures for each experimental condition. Inspection of the data indicated that normality and homogeneity of variance assumptions of analysis of variance (ANOVA) were violated. Because square-root and logarithmic transforms of the data failed to eliminate those violations we used the non-parametric Box-Type Approximation (Brunner et al. 1997) instead of standard ANOVA. The Box-Type Approximation analyzes ranks of the measurements instead of the actual measurement values (although means are presented in the "Results," the nonparametric analysis compared the ranks, not the means). The Box-Type Approximation is based on an F distribution and yields an F-like statistic, F_N, which for higher-order factorial designs with small sample sizes is more accurate than the Wald-type statistic (Akritas 1990; Akritas and Arnold 1994; Thompson 1991). An alpha level of 0.05 was used for all analyses.

Results

Figure 2 depicts COP time series and recurrence plots (Eckmann et al. 1987) for a PD (patient S1) and control participant. The figure clearly demonstrates greater COP variability (larger sway amplitude) and also a pronounced oscillatory pattern for the PD patient. The oscillations were not due to tremor—the patient did not exhibit tremor during testing, and the postural oscillations were at a much lower frequency (about 0.3 Hz) than Parkinsonian tremor

(typically 3–5 Hz; Elble and Koller, 1990). The recurrence plots were constructed by plotting a pixel at coordinates (i,j) whenever pairs of data points (i and j) were separated by less than the threshold distance of 32% of the mean Euclidean distance separating points in the reconstructed eight-dimensional phase space. The recurrence plot of the PD patient's data exhibits a greater number of short line segments parallel to the main diagonal relative to the total number of darkened pixels. Those segments indicate strings of data points (as opposed to individual data points) that repeat themselves, indicating determinism in the time series (Webber and Zbilut 1994, 1996). In order to quantify those visual patterns in the recurrence plots RQA variables were computed for each COP time series. The variable % recurrence is the percentage of darkened pixels (out of all possible coordinate pairs) in the recurrence plot. The variable % determinism is the percentage of recurrent points that fall on the diagonal line segments. Entropy refers to the irregularity of a frequency histogram in which diagonal line segments of different lengths are counted. Maxline is the length of the longest diagonal line segment, excluding the main diagonal (where $i = j$, i.e., trivial recurrence of a data point with itself). Trend refers to the paling of the recurrence plot away from the central diagonal of the plot.

Postural stability and RQA measures

The individual patients' mean postural stability and RQA measures are presented in Table 2. The SD of the AP COP was significantly higher for PD patients (mean ± 1 SD = 0.68 cm ± 0.52 cm) than for control participants (0.20 cm ± 0.12 cm) according to the Box-Type Approximation, $F_N(1,10) = 36.09$, $p < .05$. ML COP SD was also significantly higher for PD (0.82 cm ± 0.70 cm) than control participants (0.35 cm ± 0.07 cm), $F_N(1,10) = 18.05$, $p < .05$. Path length was significantly greater for PD (295.36 cm ± 96.39 cm) than control participants (208.33 cm ± 31.74 cm), $F_N(1,10) = 7.96$, $p < .05$. No other effects were significant.

Box-Type Approximations indicated that AP % recurrence was significantly greater for PD (9.09% ± 4.37%) than control participants (5.37% ± 3.41%), $F_N(1,10) = 8.20$, $p < .05$. A significant group effect was also found for AP % determinism—postural sway patterns were more deterministic, or conversely, less random, for PD (80.86% ± 28.29%) than control participants (52.68% ± 30.56%), $F_N(1,10) = 13.21$, $p < .05$. AP maxline was significantly greater for PD patients (2,138 data points ± 1,140 data points) than control participants (908 data points ± 1,165 data points), $F_N(1,10) = 8.23$, $p < .05$. Finally, AP entropy was higher for PD patients (3.57 bits ± 1.70 bits) than control participants (1.98 bits ± 1.24 bits), $F_N(1,10) = 6.82$, $p < .05$. Box-Type Approximations also revealed a significant main effect of vision for ML % recurrence, $F_N(1,10) = 6.26$, $p < .05$. Recurrence was greater with eyes open (10.11% ± 2.85%) than closed (7.42% ± 3.64%).

Table 2 Mean postural sway measures (averaged across vision and cognitive task conditions) for individual patients

Measure	S1	S2	S3	S4	S5	S6
AP SD (cm)	0.28	0.81	0.43	0.67	0.57	2.20
ML SD (cm)	0.16	1.62	0.46	0.51	0.40	0.92
Path length (cm)	352.44	413.52	374.40	237.13	210.60	184.08
AP% recurrence	6.17	5.85	6.38	6.01	16.22	15.35
ML% recurrence	9.07	2.08	8.02	8.26	15.04	12.07
AP% determinism	91.71	45.21	77.87	94.83	92.92	99.42
ML% determinism	97.18	24.75	79.53	93.78	91.87	98.06
AP% entropy	3.61	1.64	2.67	4.06	3.09	6.92
ML% entropy	5.10	0.92	2.87	3.87	3.01	5.61
AP% maxline	2,820	475	1,216	2,820	2,760	2,820
ML% maxline	2,820	23	1,612	2,820	2,733	2,820
AP% trend	−1.71	−5.34	−3.69	−2.02	−8.83	−8.55
ML% trend	−3.29	−1.08	−5.59	−1.94	−5.22	−3.96

SD, standard deviation

Cognitive performance

Cognitive task performance was evaluated in terms of the number of correct responses. Performance did not differ across groups according to a paired t-test ($p > 0.05$; PD group: 77.13% correct; control group: 75.00% correct). Performance did not differ as a function of shape rotation (72.92% and 79.17% correct for the rotated and non-rotated conditions, respectively) according to a paired t-test ($p > 0.05$).

Discussion

AP and ML COP SD and COP path length were greater for PD patients than controls. Overall, there was a higher level of COP activity or variability for PD participants, a result which is consistent with Mitchell et al.'s (1995) diffusion coefficient (D) results. Those results could be interpreted as suggesting a greater degree of neuromotor noise for PD patients (cf. Maurer et al. 2004). However, the RQA results suggest that the amount of variability of postural sway in PD should not be equated with an increase in random neuromotor noise (Riley and Turvey 2002). Novel findings obtained using RQA in this study were greater % recurrence, % determinism, maxline, and entropy in the AP (but not ML) postural sway of PD patients. Those findings indicate that overall the AP COP time series of PD patients were not more noisy than the postural sway of controls, but instead exhibited strongly deterministic dynamic patterns. An exception to that group trend was patient S2, who exhibited different COP measures (in particular, lower % determinism, entropy, and maxline, especially for ML sway) than the other patients (see Table 2). Mitchell et al. did not find evidence for greater COP determinism using SDA (they found that H did not differ between PD and control participants). Our results were generally consistent with the hypothesis that COP time series of PD patients would exhibit a loss of complexity in the form of increased determinism.

The major finding was that the COP of all but one of the PD patients exhibited a tendency to evolve over time in a more regular or patterned manner, in contrast to the COP of the control participants and to COP time series characteristic of healthy, young adults (see Riley et al. 1999). Although RQA cannot be used to explicitly identify the deterministic rule(s) according to which the COP evolved, this result is still a potentially important finding. The increase in % determinism may be a behavioral reflection of an underlying mechanism that leads to postural instability in PD. Following the reasoning of Maurer et al. (2004), who suggested that oscillatory (i.e., deterministic) sway patterns in PD could arise from variations in the motor gain in a feedback loop in their time-delay sensory feedback model, the highly deterministic COP patterns we observed could reflect an abnormal amplification of the ordinarily relatively low levels of deterministic structuring of postural sway in healthy individuals. Postural sway is the net result of a combination of factors interacting with the mechanical instability of the upright body in the gravitational field. Those factors include neuromotor noise, pulmonary and respiratory perturbations, and goal-directed muscular contractions intended to direct the body's center of mass (CM) in such a way as to maintain postural stability. The neuromuscular activity intended to maintain stability could be abnormally affected in PD—for instance, once initiated, a directed movement of the CM might be difficult to terminate, resulting in an enhancement of the effects of goal-directed postural control actions in the COP time series relative to factors such as neuromotor noise. In this case the COP would consequently exhibit a tendency for more deterministic patterns, as well as the tendency for larger short- to long-term transition times observed by Mitchell et al. (1995) and Rocchi et al. (2004).

Alternatively, the deterministic COP patterns could reflect a compensatory strategy employed by PD patients in response to postural instability (Bloem et al. 2001). If normal postural control strategies or mechanisms are unavailable to PD patients, producing a more deterministic (and perhaps more predictable) pattern of sway could allow for more efficient control of balance. This possibility is an important issue to address in future research.

Although we found group differences according to the SD and path length measures, those measures are by their nature not sensitive to the temporal evolution of postural sway, and thus may yield an incomplete or even an

inaccurate picture of postural control and postural instability in PD. It could be tempting to interpret the increase in COP SD as an increase in random COP fluctuations, given the assumption in statistics that departures from a mean value reflect random variation. Such an interpretation would be at odds with the % determinism results obtained in this study, however. The present results underscore the need to quantify the nature of the time evolution of the COP (Riley and Turvey 2002). This issue has been recognized for some time (e.g., Riccio 1993), and traditional time series methods such as power spectral analysis have been used to analyze COP data (e.g., Powell and Dzendolet 1984). However, nonstationarity of COP time series (Carroll and Freedman 1993; Newell et al. 1997; Riley et al. 1999) violates the assumptions of spectral analysis (although nonstationarity is not a problem for time-frequency analysis, a time-windowed variant of spectral analysis; Schumann et al. 1995). RQA does not assume stationarity—nor linearity, which both standard spectral analysis and time-frequency analysis do assume—nor any particular distribution of data (Webber and Zbilut 1994, 1996). Moreover, RQA has demonstrated greater sensitivity than spectral analysis in detecting neuromotor state changes (Webber et al. 1995). RQA thus seems to hold promise as a valuable tool for characterizing behavior associated with PD and other movement disorders.

The results of this study and of another recent study that employed RQA (Schmit et al. in press) provide a useful frame of reference for evaluating the concept of postural instability. Schmit et al. found that elite ballet dancers—a group with exceptional balance skills and who participated in specific balance training exercises over long periods of time—exhibited postural sway that was less nonlinearly auto-correlated (lower recurrence), less mathematically stable (lower maxline), less irregular (lower entropy), and more stationary (lower absolute trend) than a control group of track athletes who were physically fit but who lacked specific balance training. We found almost the opposite spectrum of results for PD patients (relative to healthy, elderly control participants): greater % recurrence, greater % determinism, greater maxline, and greater entropy. Although a number of procedural differences between these studies prohibit a direct quantitative comparison of the two sets of results, when considered together these studies paint a potentially revealing picture how postural stability is reflected in COP dynamics.

An important question is whether quantitative methods such as RQA can be used detect postural abnormalities earlier than commonly employed clinical methods, such as the retropulsion test. If postural abnormalities can be accurately and reliably detected before balance problems are prominent, it may be possible to initiate balance training interventions to delay the onset of postural instability in PD. It will be necessary to conduct larger-scale studies to determine whether RQA serves as a sensitive and specific predictor of postural instability associated with PD.

Static posturography and RQA could also serve as quantitative methods for evaluating PD treatments, such as pallidotomy or deep-brain electrical stimulation (DBS). Pallidotomy seems to result in better postural responses to perturbations than do pharmacological interventions (Bronte-Stewart et al. 2002; Melnick et al. 1999). Since those studies employed dynamic posturography, it remains to be seen whether static posturography might be a useful method for quantifying the effectiveness of pallidotomy. Studies employing static posturography have revealed that DBS appears to alleviate postural instability associated with PD (Rocchi et al. 2002; Maurer et al. 2003). A question that remains largely unaddressed is whether those post-intervention reductions of sway variability are accompanied by changes in the dynamic patterns of postural sway. Rocchi et al. (2004) (see also Rocchi et al. 2002) showed that DBS may reduce stochastic COP activity (equivalent to the D parameter in Mitchell et al. 1995), but might increase the transition point between the shorter- and longer-term regimes, relative to when the same patients received no treatment. RQA could be used to determine whether treatments such as pallidotomy or DBS eliminate the increased COP determinism we found to be associated with PD and result in more irregular COP time series that more closely resemble those of healthy individuals.

Individual differences in COP dynamics

As can be seen in Table 2, patient S2 exhibited a different spectrum of sway parameters than the other PD patients. Patient S2 was the oldest patient in the sample, which suggests age may have contributed to this pattern of results. To assess that possibility we computed the correlation of age with each of the dependent measures in the study. We found that age was not significantly correlated with any of the COP measures. This suggests that age, per se, may not have been responsible for that patient's pattern of results. No other clinical features distinguished that patient from the others, so it remains unclear why that patient exhibited different COP patterns than the other patients. It will be important in future research employing larger samples of PD patients to determine if instances of such individual differences in COP dynamics correlate with the presence of certain patterns of symptoms and/or with factors such as specific genetic abnormalities exhibited by some PD patients (see, e.g., Mouradian 2002).

Effects of vision and cognitive task

When vision was unavailable ML % recurrence was lower for both groups. Riley et al. (in press) observed the same effect in two experiments that employed young, healthy participants. In contrast to previous results (Bronstein et al. 1990), we did not find evidence for an increased reliance on vision by PD patients. We also did not replicate the well-known effect of greater COP variability and path length with eyes closed relative to eyes open conditions.

There were no effects of the cognitive task. Previous studies indicated that cognitive load causes balance impairments for healthy, elderly individuals (see review by Woollacott and Shumway-Cook 2002) and people with PD (Marchese et al. 2003; Morris et al. 2000). Our task may not have placed sufficient demand on participants to produce a noticeable effect on postural sway, or perhaps the task did not require continuous visualization over the entire 30 s data collection period and hence did not have a prolonged or salient effect on sway. However, the cognitive task accuracy rate was only about 75%, suggesting the task was somewhat challenging. It is possible that no effect was found because the most cognitively challenging part of our task occurred after postural data collection ceased—we collected data during the visualization period, which should have required visual working memory, but the decision-making portion of the task (when participants had to decide if the new shape was the same shape that they had visualized, which occurred after postural data collection) may have induced a greater amount of cognitive load than visualization. It is also possible that our visuo-spatial cognitive task simply may not interact with postural control in PD, but that other types of cognitive activity would.

Another possibility, however, is that features of cognitive task procedures in previous studies may have led to unintended effects that were unrelated to cognitive demand. For instance, backward counting (the task employed by Marchese et al. 2003) requires participants to vocalize during cognitive performance, but not during no-task control conditions. The fact that vocalization may cause biomechanical and respiratory artifacts in postural sway (Dault et al. 2003) could explain why postural sway was affected by performing backward counting. In contrast, our task did not require vocalization, and did not induce additional balance impairments. Whether or not cognitive load magnifies balance problems in individuals with PD remains an open and important question.

Conclusion

We found that the COP time series of PD patients receiving dopamine therapies exhibited a loss of complexity in the form of assuming a more rigid deterministic patterning, compared to the COP time series of healthy, elderly control participants (patient S2 was an exception, however). We also found that the COP was more variable and traveled a larger distance for PD patients relative to control participants. Previous studies have yielded inconsistent results with

respect to postural sway variability measures—postural sway variability was reduced for PD patients in some studies (Horak et al. 1992; Schieppati and Nardone 1991) but increased in others (Contin et al. 1996; Mitchell et al. 1995; Rocchi et al. 2002; Viitasalo et al. 2002). The reasons for those inconsistent results are not clear, but may include differences across the studies in the inclusion criteria, experimental protocols, and pharmacological conditions of patients. Additional research is needed to determine whether reliable differences between PD patients and control participants can be identified using RQA. We observed pronounced group differences in our study, despite the small sample we used, the considerable variability observed for the dependent measures, and that one patient exhibited quite a different pattern of results than the other five patients. It will be important to determine whether or not our results generalize to a larger sample and to a sample that includes patients who represent a broader range of PD severity.

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Fig. 1 A schematic of the experimental procedure. Participants stood on the force platform facing a monitor. The procedure for cognitive task trials is depicted. The left panel depicts the presentation of the cognitive task stimuli, the middle depicts the 30 s of data collection, and the right depicts the participant's cognitive response after data collection ceased. For the no-task control condition no figures were displayed and no verbal responses were obtained; participants simply stood relaxed for 30 s without a cognitive imperative

Fig. 2 Anterior-posterior center of pressure (COP) time series (*left*) and recurrence plots of the same time series (*right*) for PD (*top*) and control (*bottom*) participants. The oscillatory character of the PD patient's (S1 from Table 1) time series is representative of the increase in deterministic structure revealed by RQA, although not all patients exhibited such a pronounced oscillatory pattern. That deterministic structure is apparent in the recurrence plot in the form of diagonal line segments parallel to the main diagonal for the PD patient's data. The control participant's recurrence plot also contains diagonal line segments, indicating some degree of deterministic structure in that person's COP time series as well. However, the control participant's recurrence plot also contains a large number of isolated pixels, indicating lone data points that recurred due to chance, whereas the PD patient's recurrence plot contains comparatively fewer such points